I U C L I D

D a t a s e t

Existing Chemical	Substance ID: 96-29-7
CAS No.	96-29-7
EINECS Name	butanone oxime
EINECS No.	202-496-6
Molecular Formula	C4H9NO

Dataset created by: EUROPEAN COMMISSION – European Chemicals Bureau

This dossier is a compilation based on data reported by the European Chemicals Industry following 'Council Regulation (EEC) No. 793/93 on the Evaluation and Control of the Risks of Existing Substances'. All (non-confidential) information from the single datasets, submitted in the IUCLID/HEDSET format by individual companies, was integrated to create this document.

The data have not undergone any evaluation by the European Commission.

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1.0.1 OECD and Company Information

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1.0.2 Location of Production Site

-

1.0.3 Identity of Recipients

-

1.1 General Substance Information

Substance type: organic
Physical status: liquid

Substance type: organic
Physical status: solid

1.1.1 Spectra

-

1.2 Synonyms

2-Butanone, oxime (6CI, 8CI, 9CI)
Source: BASF AG Ludwigshafen

2-butanonoxim
Source: VOS B.V. Alphen aan den Rijn

2-Butanonoxim
Source: BASF AG Ludwigshafen

2-Butoxime
Source: BASF AG Ludwigshafen

2-butoxime, 2-butanonoxim, ethyl methyl ketone oxime, ethyl methyl ketoxime, MEK-oxime, MEKO.
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

Butanonoxim
Source: VOS B.V. Alphen aan den Rijn

Ethyl methyl ketone oxime
Source: BASF AG Ludwigshafen

Ethyl methyl ketoxime
Source: BASF AG Ludwigshafen

Ethylmethylketoxim
Source: TRANSOL Chemiehandel GmbH Essen

Mek-oxim
Source: VOS B.V. Alphen aan den Rijn

MEK-oxime
Source: BASF AG Ludwigshafen

MEKO
Source: TRANSOL Chemiehandel GmbH Essen

Methyl ethyl hetoxime
Source: MB SVEDA AB Malmö

Methyl ethyl ketone oxime
Source: BASF AG Ludwigshafen

METHYL ETHYL KETOXIME
Source: SERVO DELDEN BV DELDEN

Methyl ethyl ketoxime
Source: Elementis Specialties Birtley, County Durham
BASF AG Ludwigshafen

Methylethylketoxim
Source: TRANSOL Chemiehandel GmbH Essen

Methylethylketoxim, Ethylmethylketoxim
Source: B.V. CONSOLCO Amsterdam

METILETILCETOXIMA
Source: UNION DERIVAN S.A. VILADECANS

1.3 Impurities

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1.4 Additives

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1.5 Quantity

Quantity 10 000 – 50 000 tonnes

1.6.1 Labelling

Labelling: as in Directive 67/548/EEC
Symbols: Xi
E
Specific limits: no data
R–Phrases: (36) Irritating to eyes
(43) May cause sensitization by skin contact
S–Phrases: (2) Keep out of reach of children
(23) Do not breathe ...
(24) Avoid contact with skin

1.6.2 Classification

Classification: as in Directive 67/548/EEC
Class of danger: irritating
R–Phrases: (36) Irritating to eyes

Classification: as in Directive 67/548/EEC
Class of danger:
R–Phrases: (43) May cause sensitization by skin contact

1.7 Use Pattern

Type: type
Category: Non dispersive use

Type: type
Category: Use resulting in inclusion into or onto matrix

Type: type
Category: Wide dispersive use

Type: industrial
Category: Basic industry: basic chemicals

Type: industrial
Category: Paints, lacquers and varnishes industry

Type: use
Category: Solvents

Type: use
Category: Stabilizers

Type: use
Category: Viscosity adjustors

Type: use
Category: other: Antihautmittel

Type: use
Category:

Type: use
Category: other

1.7.1 Technology Production/Use

-

1.8 Occupational Exposure Limit Values

Type of limit: MAK (DE)
Limit value:
Remark: Kein MAK-Wert festgelegt
Source: BASF AG Ludwigshafen

(1)

Type of limit: TLV (US)
Limit value: 10 other
Remark: Opmerkingen: andere = ppm
Source: B.V. CONSOLCO Amsterdam

Type of limit: other
Limit value: 1 mg/m3
Remark: DSM advise provisional Occupational Exposure Limit Time Weighted Average (8hrs): 1 mg/m3.
Source: DSM Special Products B.V. Geleen

Type of limit:
Limit value:
Remark: SERVO/DSM advise provisional Occupational Exposure Limit, Time Weighted Average (8hrs): 10 mg/m3 (3 ppm).
Source: SERVO DELDEN BV DELDEN

Type of limit:
Limit value:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

1.9 Source of Exposure

Remark: Production from hydroxylamine and 2-butanone by oximation in closed system.
Exposure-sources: - drumming and filling of containers-tankcars
- at production of paints, lacquers, oxime-silanes and oxime-silicone sealents
- at industrial or do-it yourself use of paints, lacquers, oxime-silanes and oxime-silicone sealents

Source: SERVO DELDEN BV DELDEN

Remark: Geen blootstelling bij produktie: gesloten systeem.
Blootstellingsbronnen: - bij tappen in vaten of afvullen van containers/tankauto's
- bij de produktie van verven en lakken
- bij industrieel of huishoudelijk gebruik van verven en lakken

Source: SERVO DELDEN BV DELDEN

Remark: Production from hydroxylamine and 2-butanone by oximation in closed systems. Personal sampling indicates low exposures.
Source: DSM Special Products B.V. Geleen

Remark: envasado y posterior manipulación
Source: UNION DERIVAN S.A. VILADECANS

1.10.1 Recommendations/Precautionary Measures

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1.10.2 Emergency Measures

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1.11 Packaging

-

1.12 Possib. of Rendering Subst. Harmless

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1.13 Statements Concerning Waste

-

1.14.1 Water Pollution

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1.14.2 Major Accident Hazards

Legislation: Stoerfallverordnung (DE)
Substance listed: no
Source: BASF AG Ludwigshafen

(2)

1.14.3 Air Pollution

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1.15 Additional Remarks

Remark: not classified for road, air and sea–transport
Source: SERVO DELDEN BV DELDEN

Remark: Product is offered in bulk and in drums.
RID: 3/32c
ADR: 3/32c
Inland waterways: ADNR: 111a,4.
Free for air and sea.
Source: DSM Special Products B.V. Geleen

1.16 Last Literature Search

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1.17 Reviews

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1.18 Listings e.g. Chemical Inventories

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2.1 Melting Point

Value: = -20 degree C
Remark: Thermische Zersetzung: > 150 Grad C
Bildung von Hydroxylamin moeglich.
Source: BASF AG Ludwigshafen
(3)

Value: ca. -17 degree C
Decomposition: no
Sublimation: no
Method: other
GLP: no
Remark: Methode: DGF-C-IV-3A
Source: SERVO DELDEN BV DELDEN

Value: = -30 degree C
Decomposition: no
Sublimation: no
Method: other
Year: 1988
GLP: no data
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen
(4)

Value:
Remark: no adecuado
Source: UNION DERIVAN S.A. VILADECANS

2.2 Boiling Point

Value: ca. 152 degree C at 1013 hPa
Decomposition: ambiguous
Method: other
GLP: no
Source: SERVO DELDEN BV DELDEN

Value: ca. 153 degree C
Decomposition: no
Method: other
GLP: yes
Source: UNION DERIVAN S.A. VILADECANS

Value: = 152 degree C at 1013 hPa
Decomposition: yes
Method: other
GLP: no data
Remark: Decomposition will occur above 100 C. When heated, decomposition will be promoted by contamination with acids and metals.
Source: SERVO DELDEN BV DELDEN
(5)

Value: = 153 degree C hPa
Decomposition: yes
Method: other
Year: 1988
GLP: no data
Remark: Decomposition will occur above 100 C. When heated, decomposition will be promoted by contamination with acids and metals.
Source: DSM Special Products B.V. Geleen

(6)

2.3 Density

Type: relative density
Value: ca. .92 g/cm3 at 20 degree C
Method: other
GLP: no data
Source: SERVO DELDEN BV DELDEN

(4)

Type: density
Value: ca. .92 g/cm3 at 20 degree C
Method: other
GLP: yes
Source: UNION DERIVAN S.A. VILADECANS

Type: relative density
Value: = .9232 g/cm3 at 20 degree C
Method: other
Year: 1988
GLP: no data
Source: DSM Special Products B.V. Geleen

(4)

Type: density
Value: ca. 920 kg/m3 at 20 degree C
Method: other
GLP: no
Remark: ASTM D1298, DIN 51757
Source: SERVO DELDEN BV DELDEN

Type: density
Value: = .915 g/cm3
Method: other: DIN 53 217
Source: BASF AG Ludwigshafen

(3)

2.3.1 Granulometry

-

2.4 Vapour Pressure

Value: ca. 3.5 hPa at 20 degree C
Method: other (measured)
GLP: no
Remark: SERVO Material Safety Data Sheet
Source: SERVO DELDEN BV DELDEN

Value: ca. 3.5 hPa at 20 degree C
Method: other (measured)
GLP: no
Source: SERVO DELDEN BV DELDEN

Value: = 4.4 hPa at 20 degree C
Source: BASF AG Ludwigshafen
(3)

Value: = 13.3 hPa at 50 degree C
Method: other (measured)
Year: 1988
GLP: no data
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen
(7)

Value: ca. 13.3 hPa at 50 degree C
Method: other (measured)
GLP: yes
Source: UNION DERIVAN S.A. VILADECANS

Value: = 19.5 hPa at 50 degree C
Source: BASF AG Ludwigshafen
(3)

2.5 Partition Coefficient

log Pow: = .59 at 20 degree C
Method: other (measured)
Year: 1988
GLP: no data
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen
(4)

log Pow: = .65 at 25 degree C
Method: OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year: 1988
GLP: no data
Source: SERVO DELDEN BV DELDEN
(8)

log Pow: .65 at 25 degree C
Method: OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year: 1988
GLP: no data
Source: DSM Special Products B.V. Geleen
(9)

log Pow: = .65 at 25 degree C
Method: OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year:
Source: BASF AG Ludwigshafen
(10)

log Pow:
Method:
Year:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

2.6.1 Water Solubility

Value: = 100 g/l at 20 degree C
pH: = 6.5 at 114 g/l and 20 degree C
Method: other
Year: 1988
GLP: no data
Source: DSM Special Products B.V. Geleen
(11)

Value: ca. 110 g/l at 20 degree C
pH: ca. 6.5 at 110 g/l and 20 degree C
Method: other
Year: 1988
GLP: no data
Source: SERVO DELDEN BV DELDEN
(11)

Value: ca. 110 g/l at 20 degree C
Qualitative: soluble
pH: ca. 6.5 at 110 g/l and 20 degree C
Method: other
GLP: no
Source: SERVO DELDEN BV DELDEN

Value: ca. 110 g/l at 20 degree C
Source: UNION DERIVAN S.A. VILADECANS

Value: ca. 114 g/l at 20 degree C
pH: = 6.5 at 114 g/l and 20 degree C
Source: BASF AG Ludwigshafen
(3)

2.6.2 Surface Tension

-

2.7 Flash Point

Value: = 62 degree C
Type: closed cup
Method: other
Year: 1988
GLP: no data
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen
(11)

Value: ca. 62 degree C
Type: closed cup
Method: other
Year:
GLP: no
Remark: PENSKY MARTENS CC, ASTM D93
Source: SERVO DELDEN BV DELDEN

Value: ca. 62 degree C
Type: open cup
Method: other
Year:
GLP: yes
Source: UNION DERIVAN S.A. VILADECANS

Value: = 62 degree C
Type:
Method: other: ISO 3679
Year:
Source: BASF AG Ludwigshafen
(3)

2.8 Auto Flammability

Value: = 315 degree C
Method: other
GLP: no data
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen
(12)

Value: ca. 315 degree C at 1013 hPa
Method: Directive 84/449/EEC, A.15 "Auto-flammability of volatile liquids or gases"
GLP: no
Source: SERVO DELDEN BV DELDEN

Value: ca. 315 degree C
Method: other
GLP: yes
Source: UNION DERIVAN S.A. VILADECANS

Value: = 315 degree C
Method: other: DIN 51 794
Source: BASF AG Ludwigshafen

(3)

2.9 Flammability

Result: non flammable
Method: Directive 84/449/EEC, A.13 "Flammability (solids and liquids)"
GLP: no
Source: SERVO DELDEN BV DELDEN

Result:
Remark: No data available.
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

Result:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

2.10 Explosive Properties

Result: not explosive
Method: Directive 84/449/EEC, A.14 "Explosive properties"
Remark: Explosion Limits in air: 3.1 – 50 Volume % at 60 C and 1013 hPa.
Source: SERVO DELDEN BV DELDEN

(12)

Result: not explosive
Method: Directive 84/449/EEC, A.14 "Explosive properties"
GLP: no
Source: SERVO DELDEN BV DELDEN

Result:
Remark: Explosion Limits in air: 3.1 – 50 Volume % at 60 C and 1013 hPa.
Source: DSM Special Products B.V. Geleen

(12)

Result:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

Result:
Remark: Explosionsgrenzen in Luft: 3,1 - 50 Vol. % bei 60 Grad C und 1013 hPa
Source: BASF AG Ludwigshafen

(3)

2.11 Oxidizing Properties

Result: no oxidizing properties
Method: Directive 84/449/EEC, A.17 "Oxidizing properties"
Source: SERVO DELDEN BV DELDEN

Result: no oxidizing properties
Method: Directive 84/449/EEC, A.17 "Oxidizing properties"
GLP: no
Source: SERVO DELDEN BV DELDEN

Result:
Remark: el producto no es comburente
Source: UNION DERIVAN S.A. VILADECANS

2.12 Additional Remarks

Remark: When heated strong exothermic reactions may occur.
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

Remark: Gefaehrliche Reaktionen: bei Erwaermung stark exotherme Reaktion moeglich.
Source: BASF AG Ludwigshafen

(3)

3.1.1 Photodegradation

Type:
Method:
Year: **GLP:**
Test substance:
Remark: No data are available on the photodegradation of 2–butanone oxime. However, it is expected that it will be photooxidised in the atmosphere.
Source: SERVO DELDEN BV DELDEN

Type:
Method:
Year: **GLP:**
Test substance:
Remark: No data are available on the photodegradation of 2–butanone oxime. However, it is expected that it will be photooxidised in the atmosphere.
Source: DSM Special Products B.V. Geleen

Type:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

3.1.2 Stability in Water

Type:
Method:
Year: **GLP:**
Test substance:
Remark: No data available.
Stability against acids and bases is limited.
At hydrolysis hydroxylamine and 2–butanone are formed.
Source: SERVO DELDEN BV DELDEN

Type:
Method:
Year: **GLP:**
Test substance:
Remark: Stabiliteit tegen zuren en basen is beperkt. Bij hydrolyse worden hydroxylamine en 2–butanon gevormd.
Waarden zijn echter niet voor handen.
Source: SERVO DELDEN BV DELDEN

Type:
Method:
Year: **GLP:**
Test substance:
Remark: No data available.
Source: DSM Special Products B.V. Geleen

Type:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

3.1.3 Stability in Soil

Type: **Radiolabel:**
Concentration:
Cation exch. capac.
Microbial biomass:
Method:
Year: **GLP:**
Test substance:
Remark: No data available.
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

Type: **Radiolabel:**
Concentration:
Cation exch. capac.
Microbial biomass:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

3.2 Monitoring Data (Environment)

Type of measurement: concentration at contaminated site
Medium: air
Remark: Experiments with MEKO–containing paint in a hall of an office building by four painters during a 4–hours period, gave an average air concentration of 0.27–0.46 ppm.
Source: SERVO DELDEN BV DELDEN
(13)

Type of measurement: concentration at contaminated site
Medium: air
Remark: Experiments with MEKO–containing paint in a hall of an office building by four painters during a 4–hours period, gave an average air concentration of 0.27–0.46 ppm.
Source: DSM Special Products B.V. Geleen
(14)

Type of measurement:
Medium:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

3.3.1 Transport between Environmental Compartments

Type:
Media:
Method:
Year:
Remark: No data available.
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

Type:
Media:
Method:
Year:
Source: SERVO DELDEN BV DELDEN

Type:
Media:
Method:
Year:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

3.3.2 Distribution

Media:
Method:
Year:
Remark: No data available.
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

Media:
Method:
Year:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

3.4 Mode of Degradation in Actual Use

Remark: Hydrolysis to hydroxylamine and 2–butanone.
Further decomposition–route unknown.
No data available.
Source: SERVO DELDEN BV DELDEN

Remark: Hydrolyse tot 2-butanon en hydroxylamine. Verdere afbraakroute onbekend.
Source: SERVO DELDEN BV DELDEN

Remark: No data available.
Source: DSM Special Products B.V. Geleen

Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge
Concentration: 400 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: ca. 70 % after 14 day
Result: readily biodegradable
Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: **GLP:** no
Test substance: other TS
Source: SERVO DELDEN BV DELDEN

Type: aerobic
Inoculum: activated sludge
Concentration: 400 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: ca. 70 % after 14 day
Result: readily biodegradable
Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Source: SERVO DELDEN BV DELDEN

Type: aerobic
Inoculum: activated sludge
Concentration: 30 mg/l related to Test substance
Degradation: = 25 % after 28 day
Result: inherently biodegradable
Method: other
Year: 1992 **GLP:** yes
Test substance: other TS
Remark: Degree of biodegradation was 24.7% by BOD after 28 days. Testsubstance concentration 30 mg/l and activated sludge concentration 100 mg/l (as suspended solid).
Source: SERVO DELDEN BV DELDEN

(15)

Type: aerobic
Inoculum: activated sludge
Concentration: 30 mg/l related to Test substance
Degradation: = 25 % after 28 day
Result: inherently biodegradable
Method: other
Year: 1992 **GLP:** yes
Test substance: other TS
Remark: Degree of biodegradation was 24.7% by BOD after 28 days. Testsubstance concentration 30 mg/l and activated sludge concentration 100 mg/l (as suspended solid).
Source: DSM Special Products B.V. Geleen

(16)

Type: aerobic
Inoculum: activated sludge
Concentration: 30 mg/l related to Test substance
Degradation: = 24.7 % after 28 day
Method: other: MITI-Test (BOD of THOD)
Year: **GLP:**
Test substance:
Source: BASF AG Ludwigshafen
Test condition: Concentration of sludge: 100 mg/l

(17)

Type: aerobic
Inoculum: other: Belebtschlamm der BASF-Klaeranlage
Concentration: related to DOC (Dissolved Organic Carbon)
Degradation: = 70 % after 18 day
Result: other: gut eliminierbar
Method: other: Standversuch
Year: **GLP:**
Test substance:
Source: BASF AG Ludwigshafen

(18)

Type: aerobic
Inoculum: other
Concentration: related to DOC (Dissolved Organic Carbon)
Degradation: = 70 % after 18 day
Result: readily biodegradable
Method:
Year: **GLP:**
Test substance:
Remark: Inoculum was of the BASF water purification plant.
Source: SERVO DELDEN BV DELDEN

(19)

Type: aerobic
Inoculum: other
Concentration: related to DOC (Dissolved Organic Carbon)
Degradation: = 70 % after 18 day
Result: readily biodegradable
Method:
Year: **GLP:**
Test substance:
Remark: Inoculum was of the BASF water purification plant.
Source: DSM Special Products B.V. Geleen

(20)

Type:
Inoculum:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

3.6 BOD5, COD or BOD5/COD Ratio

Remark: Not relevant see 3.5
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

3.7 Bioaccumulation

Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 42 day at 25 degree C
Concentration: 2 mg/l
BCF: ca. .5 - .6
Elimination:
Method: OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year: **GLP:**
Test substance:
Source: BASF AG Ludwigshafen
Test condition: Lipid: 4.9% (av.)

(17)

Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 42 day at 25 degree C
Concentration: .2 mg/l
BCF: < 2.5 - 5.8
Elimination:
Method: OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year: **GLP:**
Test substance:
Source: BASF AG Ludwigshafen
Test condition: Lipid: 4.9% (av.)

(17)

Species: Oryzias latipes (Fish, fresh water)
Exposure period: 42 day at 25 degree C
Concentration: 2 mg/l
BCF: = .5 - .6
Elimination: no
Method: OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year: 1992 **GLP:** yes
Test substance: other TS
Remark: MITI test. Bioaccumulation in fish. The test was conducted until the BCF reached to an equilibrium. Mean lipid content of the same lot of fish was 4.9%. The BCF at the equilibrium was listed.
Source: SERVO DELDEN BV DELDEN

(21)

Species: Oryzias latipes (Fish, fresh water)
Exposure period: 42 day at 25 degree C
Concentration: 2 mg/l
BCF: = .5 - .6
Elimination: no
Method: OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year: 1992 **GLP:** yes
Test substance: other TS
Remark: MITI test. Bioaccumultion in fish. The test was conducted untill the BCF reached to an equilibrium. Mean lipid content of the same lot of fish was 4.9% The BCF at the equilibrium was listed.
Source: DSM Special Products B.V. Geleen

(21)

Species: Oryzias latipes (Fish, fresh water)
Exposure period: 42 day at 25 degree C
Concentration: .2 mg/l
BCF: 2.5 - 5.8
Elimination: no
Method: OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year: 1992 **GLP:** yes
Test substance: other TS
Remark: Same test as mentioned in 3.7.1
Source: SERVO DELDEN BV DELDEN

(22)

Species: Oryzias latipes (Fish, fresh water)
Exposure period: 42 day at 25 degree C
Concentration: .2 mg/l
BCF: < 2.5 - 5.8
Elimination: no
Method: OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year: 1992 **GLP:** yes
Test substance: other TS
Remark: Same test as mentioned in 3.7.1
Source: DSM Special Products B.V. Geleen

(22)

Species:
Exposure period:
Concentration:
BCF:
Elimination:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

3.8 Additional Remarks

Remark: BCF = 0.63 (calculated on basis of Kow).
Log BCF = 0.85 logKow - 0.7
Source: SERVO DELDEN BV DELDEN

(23)

Remark: BCF = 0.63 (calculated on basis of Kow).
Log BCF = 0.85 logKow - 0.7
Source: DSM Special Products B.V. Geleen

(24)

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
LC50: = 843
Method: other
Year: 1984 **GLP:** no data
Test substance: other TS
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

(25)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
NOEC: = 320
LC50: = 320 - 1000
Method: other
Year: 1982 **GLP:** no
Test substance: other TS
Remark: BASF in-house test DIN 38 412.
Source: SERVO DELDEN BV DELDEN

(26)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no data
NOEC: = 320
LC50: = 320 - 1000
Method: other
Year: 1982 **GLP:** no
Test substance: other TS
Remark: BASF in-house test DIN 38 412.
Source: DSM Special Products B.V. Geleen

(27)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** yes
NOEC: 320
LC50: 320 - 1000
Method: other: nach Guideline DIN 38 412 "Bestimmung der Wirkung von Wasserinhaltsstoffen auf Fische - Fischtest"
Year: 1982 **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen

(28)

Type: static
Species: Poecilia reticulata (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no
LC50: = 760
Method: ISO 7346/1-3
Year: 1989 **GLP:** no
Test substance: other TS
Remark: DSM in-house test.
Source: SERVO DELDEN BV DELDEN

(29)

Type: static
Species: Poecilia reticulata (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l **Analytical monitoring:** no
LC50: = 760
Method: ISO 7346/1-3
Year: 1989 **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Remark: DSM in-house test.
Source: DSM Special Products B.V. Geleen

(29)

Type: static
Species: other
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** yes
LC50: = 560
Method: other
Year: 1992 **GLP:** yes
Test substance: other TS
Remark: MITI test. Acute toxicity test for orange red-killifish.
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

(30)

Type:
Species:
Exposure period:
Unit: **Analytical monitoring:**
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

4.2 Acute Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC0: = 500
EC50: > 500
EC100: > 500
Method: Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
Year: 1988 **GLP:** no data
Test substance: other TS
Remark: BASF in-house test with Daphnia magna Straus.
Source: SERVO DELDEN BV DELDEN

(31)

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC0: = 500
EC50: > 500
EC100: > 500
Method: Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
Year: 1988 **GLP:** no data
Test substance: other TS
Remark: BASF in house test with Daphnia magna Straus.
Source: DSM Special Products B.V. Geleen

(32)

Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC50: = 750
Method: other
Year: 1986 **GLP:** no data
Test substance: other TS
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

(33)

Species: other: Daphnia magna Straus
Exposure period: 48 hour(s)
Unit: mg/l **Analytical monitoring:**
EC0: = 500
EC50: > 500
EC100: > 500
Method: Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
Year: **GLP:**
Test substance:
Remark: Werte gelten ebenso fuer 24-h-Test.
Source: BASF AG Ludwigshafen

(34)

Species:
Exposure period:
Unit: **Analytical monitoring:**
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus sp. (Algae)
Endpoint: growth rate
Exposure period:
Unit: mg/l **Analytical monitoring:** no data
LOEC: = 1000
Method: other
Year: 1968 **GLP:** no data
Test substance: other TS
Source: SERVO DELDEN BV DELDEN

(35)

Species: Scenedesmus sp. (Algae)
Endpoint: growth rate
Exposure period:
Unit: mg/l **Analytical monitoring:** no data
LOEC: = 1000
Method: other
Year: 1968 **GLP:** no data
Test substance: other TS
Source: DSM Special Products B.V. Geleen

(36)

Species: Scenedesmus sp. (Algae)
Endpoint:
Exposure period:
Unit: g/l **Analytical monitoring:**
LOEC: 1
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Source: SERVO DELDEN BV DELDEN

(37)

Species: Scenedesmus subspicatus (Algae)
Endpoint:
Exposure period: 72 hour(s)
Unit: mg/l **Analytical monitoring:**
EC50: = 83
ec90 : = 121
Method: other: Algentest in Anlehnung an UBA (DIN 38 412/9)
Year: **GLP:**
Test substance:
Remark: EC20(72 h)= 55 mg/l
Source: BASF AG Ludwigshafen

(38)

Species: Scenedesmus subspicatus (Algae)
Endpoint:
Exposure period: 72 hour(s)
Unit: mg/l **Analytical monitoring:**
EC50: = 83
EC100 : = 121
Method:
Year: **GLP:**
Test substance:
Remark: BASF in-house test DIN 38 412/9. EC20 72 hours = 55 mg/l
Source: SERVO DELDEN BV DELDEN

(39)

Species: Scenedesmus subspicatus (Algae)
Endpoint:
Exposure period: 72 hour(s)
Unit: mg/l **Analytical monitoring:**
EC50: = 83
EC100 : = 121
Method:
Year: **GLP:**
Test substance:
Remark: BASF in house test DIN 38 412/9. EC20 72 hours = 55 mg/l
Source: DSM Special Products B.V. Geleen

(40)

Species:
Endpoint:
Exposure period:
Unit: **Analytical monitoring:**
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: Pseudomonas putida (Bacteria)
Exposure period: 17 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC10: = 177
EC50: = 281
EC90 : = 544
Method: other
Year: 1988 **GLP:** no data
Test substance: other TS
Remark: Growth inhibition. BASF in-house test.
Source: SERVO DELDEN BV DELDEN

(41)

Type: aquatic
Species: Pseudomonas putida (Bacteria)
Exposure period: 17 hour(s)
Unit: mg/l **Analytical monitoring:** no data
EC10: = 177
EC50: = 281
EC90 : = 544
Method: other
Year: 1988 **GLP:** no data
Test substance: other TS
Remark: Growth inhibition. BASF in house test.
Source: DSM Special Products B.V. Geleen

(41)

Type: aquatic
Species: Pseudomonas sp. (Bacteria)
Exposure period:
Unit: mg/l **Analytical monitoring:** no data
EC0: > 500
Method: other
Year: 1968 **GLP:** no data
Test substance: other TS
Remark: See 4.3
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

Type: aquatic
Species: Pseudomonas sp. (Bacteria)
Exposure period:
Unit: g/l **Analytical monitoring:**
LOEC : .63
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: SERVO DELDEN BV DELDEN

(42)

Type: aquatic
Species: other protozoa
Exposure period:
Unit: g/l **Analytical monitoring:**
LOEC : 2.5
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: SERVO DELDEN BV DELDEN

(43)

Type:
Species: activated sludge
Exposure period:
Unit: **Analytical monitoring:**
Method:
Year: **GLP:**
Test substance:
Remark: Bei sachgemaesser Einleitung in adaptierte biologische Klaeranlagen sind keine Stoerungen der Abbauaktivitaet des Belebtschlamms zu erwarten.
Source: BASF AG Ludwigshafen

(44)

Type:
Species: Pseudomonas putida (Bacteria)
Exposure period: 17 hour(s)
Unit: mg/l **Analytical monitoring:**
EC10: = 177
EC50: = 281
EC90 : = 544
Method: other: Bakterienwachstumshemmtest nach DIN 38412 Teil 8 (Entwurf)
Year: **GLP:**
Test substance:
Source: BASF AG Ludwigshafen

(45)

Type:
Species:
Exposure period:
Unit: **Analytical monitoring:**
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

Species:
Endpoint:
Exposure period:
Unit: **Analytical monitoring:**
Method:
Year: **GLP:**
Test substance:
Remark: No data available.
On basis of the very low acute toxicity, no relevant chronic toxicity is expected.
Source: SERVO DELDEN BV DELDEN

Species:
Endpoint:
Exposure period:
Unit: **Analytical monitoring:**
Method:
Year: **GLP:**
Test substance:
Remark: No data available.
On basis of the very low acute toxicity, no relevant chronic toxicity is expected.
Source: DSM Special Products B.V. Geleen

Species:
Endpoint:
Exposure period:
Unit: **Analytical monitoring:**
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species:
Endpoint:
Exposure period:
Unit: **Analytical monitoring:**
Method:
Year: **GLP:**
Test substance:
Remark: No data available.
On basis of the very low acute toxicity, no relevant chronic toxicity is expected.
Source: SERVO DELDEN BV DELDEN

Species:
Endpoint:
Exposure period:
Unit: **Analytical monitoring:**
Method:
Year: **GLP:**
Test substance:
Remark: No data avaible.
On basis of the very low acute toxicity, no relevant chronic toxicity is expected.
Source: DSM Special Products B.V. Geleen

Species:
Endpoint:
Exposure period:
Unit: **Analytical monitoring:**
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

Type:
Species:
Endpoint:
Exposure period:
Unit:
Method:
Year: **GLP:**
Test substance:
Remark: No data available.
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

Type:
Species:
Endpoint:
Exposure period:
Unit:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

4.6.2 Toxicity to Terrestrial Plants

Species:
Endpoint:
Expos. period:
Unit:
Method:
Year: **GLP:**
Test substance:
Remark: No data available.
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

Species:
Endpoint:
Expos. period:
Unit:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

4.6.3 Toxicity to other Non–Mamm. Terrestrial Species

Species:
Endpoint:
Expos. period:
Unit:
Method:
Year: **GLP:**
Test substance:
Remark: No data available.
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

Species:
Endpoint:
Expos. period:
Unit:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

4.7 Biological Effects Monitoring

Remark: No data available.
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

4.8 Biotransformation and Kinetics

Type: animal
Remark: Pregnant mice were administered a single oral dose of 14C 2–butanoneoxime on day 14 of gestation. In addition a male mouse was administered a single oral dose of 14C 2–butanone oxime. It appears that the substance is rapidly absorbed via the oral route, and distributed intact through the body. Urine and bile contained significant activity throughout the study. Intestinal activity was minimal. This suggests that the substance is primarily excreted via the kidneys.
Source: SERVO DELDEN BV DELDEN

(46)

Type: animal
Remark: Pregnant mice were administered a single oral dose of 14C 2–butanoneoxime on day 14 of gestation. In addition a male mouse was administered a single oral dose of 14C 2–butanone oxime. It appeares that the substance is rapidly absorbed via the oral route, and distributed intact through the body. Urine and bile contained significant activity throughout the study. Intestinal activity was minimal. This sugests that the substance is primarily excreted via the kidneys.
Source: DSM Special Products B.V. Geleen

(47)

Type:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

4.9 Additional Remarks

Remark: the substance can be metabolized in–vivo in animals to 2–butanone and hydroxylamine.
Source: SERVO DELDEN BV DELDEN

(48)

Remark: the substance can be metabolized in–vivo in animals to 2–butanone and hydroxylamine.
Source: DSM Special Products B.V. Geleen

(48)

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: = 2528 mg/kg bw
Method: other
Year: 1971 **GLP:** no
Test substance: other TS
Remark: BASF in–house test.
Source: SERVO DELDEN BV DELDEN

(49)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: = 2326 mg/kg bw
Method: other
Year: 1978 **GLP:** no data
Test substance: other TS
Source: SERVO DELDEN BV DELDEN

(50)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: 3700 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: other TS
Source: SERVO DELDEN BV DELDEN

(51)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: 2400 – 3700 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Source: SERVO DELDEN BV DELDEN

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: = 930 mg/kg bw
Method: other
Year: 1986 **GLP:** no data
Test substance: other TS
Source: DSM Special Products B.V. Geleen

(52)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: = 2528 mg/kg bw
Method: other
Year: 1971 **GLP:** no
Test substance: other TS
Remark: BASF in house test.
Source: DSM Special Products B.V. Geleen

(53)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Value: ca. 2528 mg/kg bw
Method: other: BASF-Test
Year: **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen

(54)

Type:
Species:
Sex:
Number of Animals:
Vehicle:
Value:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

5.1.2 Acute Inhalation Toxicity

Type: LC0
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: = 3.6 - 4 mg/l
Method: other
Year: 1986 **GLP:** no data
Test substance: other TS
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

(55)

Type: LC100
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: ca. 5000 ppm
Method: other
Year: 1965 **GLP:** no data
Test substance: other TS
Source: SERVO DELDEN BV DELDEN

(56)

Type: LC100
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: ca. 5000 ppm
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: SERVO DELDEN BV DELDEN

(57)

Type: LC50
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: = 20 mg/l
Method: other
Year: 1986 **GLP:** no data
Test substance: other TS
Source: SERVO DELDEN BV DELDEN
(58)

Type: LC50
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: = 20 mg/l
Method: other
Year: 1986 **GLP:** no data
Test substance: other TS
Source: DSM Special Products B.V. Geleen
(59)

Type: other
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 8 hour(s)
Value: =
Method: other
Year: 1971 **GLP:** no
Test substance: other TS
Remark: 8 hour exposure of 12 rats to a MEKO saturated atmosphere at 20 C, resulted in no deaths. BASF in house test.
Source: SERVO DELDEN BV DELDEN
(60)

Type: other
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 8 hour(s)
Value: =
Method: other
Year: 1971 **GLP:** no
Test substance: other TS
Remark: 8 hour exposure of 12 rats to a MEKO saturated atmosphere at 20 C, resulted in no deaths. BASF in house test.

Source: DSM Special Products B.V. Geleen
(60)

Type: other: IRT
Species: rat
Sex:
Number of Animals:
Vehicle:
Exposure time: 8 hour(s)
Value:
Method: other: BASF-Test
Year: **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Remark: Die 8-stuendige Exposition von 12 Ratten in einer bei 20 Grad Celsius mit der Substanz gesõttigten Atmosphaere wirktebei keinem der Tiere letal.
Source: BASF AG Ludwigshafen
(61)

Type:
Species:
Sex:
Number of Animals:
Vehicle:
Exposure time:
Value:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rabbit
Sex:
Number of Animals:
Vehicle:
Value: 1000 - 2000 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: other TS
Source: SERVO DELDEN BV DELDEN
(62)

Type: LD50
Species: rabbit
Sex:
Number of Animals:
Vehicle:
Value: .2 – 1.8 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Source: SERVO DELDEN BV DELDEN

Type:
Species:
Sex:
Number of Animals:
Vehicle:
Value:
Method:
Year: **GLP:**
Test substance:
Remark: No relevant data available
Source: DSM Special Products B.V. Geleen

Type:
Species:
Sex:
Number of Animals:
Vehicle:
Value:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 521 mg/kg bw
Method: other
Year: 1971 **GLP:** no
Test substance: other TS
Remark: BASF in–house test.
Source: SERVO DELDEN BV DELDEN

(60)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 521 mg/kg bw
Method: other
Year: 1971 **GLP:** no
Test substance: other TS
Remark: BASF in house test.
Source: DSM Special Products B.V. Geleen

(60)

Type: LD50
Species: mouse
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: ca. 521 mg/kg bw
Method: other: BASF-Test
Year: **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen

(54)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Route of admin.: s.c.
Value: = 2700 mg/kg bw
Method: other
Year: **GLP:** no data
Test substance: other TS
Source: SERVO DELDEN BV DELDEN

(63)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Route of admin.: s.c.
Value: ca. 2700 mg/kg bw
Method: andere
Year: **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: SERVO DELDEN BV DELDEN

(64)

Type: LD50
Species: rat
Sex:
Number of Animals:
Vehicle:
Route of admin.: s.c.
Value: = 2700 mg/kg bw
Method: other
Year: 1989 **GLP:** no data
Test substance: other TS
Source: DSM Special Products B.V. Geleen

(65)

Type:
Species:
Sex:
Number of Animals:
Vehicle:
Route of admin.:
Value:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: moderately irritating
EC classificat.: irritating
Method: other
Year: 1989 **GLP:** no data
Test substance: other TS
Remark: Probably according to USA guidelines so 24 hour exposure of skin instead of 4 hours in EC.
Source: SERVO DELDEN BV DELDEN

(66)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.: not irritating
Method: other
Year: 1971 **GLP:** no
Test substance: other TS
Remark: BASF in house test.
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

(60)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: slightly irritating
EC classificat.: not irritating
Method: other
Year: 1978 **GLP:** no data
Test substance: other TS
Source: SERVO DELDEN BV DELDEN

(50)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: slightly irritating
EC classificat.: irritating
Method: Draize Test
Year: **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Source: SERVO DELDEN BV DELDEN

(50)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: moderately irritating
EC classificat.: irritating
Method: other
Year: 1989 **GLP:** no data
Test substance: other TS
Remark: Probably according to USA guidelines so 24 hour exposure of skin instead of 4 hours in EC.
Source: DSM Special Products B.V. Geleen

(67)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.:
Method: other: BASF-Test
Year: **GLP:** no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen

(54)

Species: rat
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: irritating
EC classificat.: irritating
Method: other
Year: 1988 **GLP:** no data
Test substance: other TS
Remark: Probably 24 hours exposure.
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

(68)

Species:
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result:
EC classificat.:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: highly irritating
EC classificat.: irritating
Method: other
Year: 1989 **GLP:** no data
Test substance: other TS
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

(69)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: irritating
EC classificat.: irritating
Method: other
Year: 1971 **GLP:** no
Test substance: other TS
Remark: BASF in house test.
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

(60)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: highly irritating
EC classificat.: irritating
Method: other
Year: 1963 **GLP:** no data
Test substance: other TS
Source: SERVO DELDEN BV DELDEN

(70)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: highly irritating
EC classificat.: irritating
Method: other
Year: **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Source: SERVO DELDEN BV DELDEN

(70)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: irritating
EC classificat.:
Method: other: BASF–Test
Year: **GLP:** no
Test substance: as prescribed by 1.1 – 1.4
Source: BASF AG Ludwigshafen

(71)

Species:
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result:
EC classificat.:
Method:
Year: **GLP:**
Test substance:

Remark: no disònible
Source: UNION DERIVAN S.A. VILADECANS

5.3 Sensitization

Type: Guinea pig maximization test
Species: guinea pig
Number of Animals:
Vehicle:
Result: sensitizing
Classification: sensitizing
Method: Directive 84/449/EEC, B.6 "Acute toxicity (skin sensitization)"
Year: 1990 **GLP:** yes
Test substance: other TS
Source: SERVO DELDEN BV DELDEN

(72)

Type: Guinea pig maximization test
Species: guinea pig
Number of Animals:
Vehicle:
Result: sensitizing
Classification: sensitizing
Method: Directive 84/449/EEC, B.6 "Acute toxicity (skin sensitization)"
Year: 1990 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Source: DSM Special Products B.V. Geleen

(72)

Type: Guinea pig maximization test
Species: guinea pig
Number of Animals:
Vehicle:
Result: sensitizing
Classification: sensitizing
Method: OECD Guide-line 406 "Skin Sensitization"
Year: 1983 **GLP:** yes
Test substance: other TS
Source: SERVO DELDEN BV DELDEN

(73)

Type: Guinea pig maximization test
Species: guinea pig
Number of Animals:
Vehicle:
Result: sensitizing
Classification: sensitizing
Method: other
Year: 1983 **GLP:** yes
Test substance: as prescribed by 1.1 - 1.4
Source: SERVO DELDEN BV DELDEN

(73)

Type:
Species:
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

5.4 Repeated Dose Toxicity

Species: rat **Sex:** male/female
Strain:
Route of admin.: inhalation
Exposure period: 28 days
Frequency of treatment: 6h/d and 5d/w
Post. obs. period:
Doses: 0.21, 1.02, 1.92, 2.57 mg/l
Control Group: yes
NOAEL: = 1.02 mg/l
LOAEL: = 1.92 mg/l
Method: other
Year: 1989 **GLP:** no data
Test substance: other TS
Remark: Study performed by DOW-Corning USA. Minor changes in hematological parameters at doses 1.92 mg/l and higher. Changes in organ weight (spleen, liver) at doses 1.92 mg/l and higher. Accumulation of iron in spleen at 1.92 mg/l and higher.
Source: SERVO DELDEN BV DELDEN

(74)

Species: rat **Sex:** male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure period: 4 weeks
Frequency of treatment: 6h/d and 5d/w
Post. obs. period:
Doses: 25, 100, 400 ppm
Control Group: yes
NOAEL: = 25 ppm
LOAEL: = 100 ppm
Method: other
Year: 1990 **GLP:** yes
Test substance: other TS
Remark: The rats were exposed by inhalation to MEKO vapour. Exposure levels were analysed and particle size distribution measured. Ten animals/sex/group were used. At 100 ppm increased methemoglobin was observed in female rats. At 400 ppm significant alterations in most hematological parameters (increased methemoglobin, increased reticulocytes, increased platelets, increased MCW and MCH, increased total leucocytes counts, in addition decreased hemoglobin, hematocrit, erythrocytes and MCHC) were observed for both male and female rats. At 400 ppm remarcable erythrocyte morphology included increased numbers of nucleated erythrocytes and polychromia, were seen in male and female rats.
At 400 ppm increased absolute and relative organ weights of liver and spleen in males and females was seen.
Source: SERVO DELDEN BV DELDEN

(75)

Species: rat **Sex:** no data
Strain:
Route of admin.: inhalation
Exposure period: geen gegevens
Frequency of treatment: geen gegevens
Post. obs. period: geen gegevens
Doses: 0, 60, 283, 533, 714 ppm
Control Group: no data specified
NOAEL: 283 ppm
Method: other
Year: 1977 **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Source: SERVO DELDEN BV DELDEN

(76)

Species: rat **Sex:** male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure period: 4 weken
Frequency of treatment: 6 uur/dag, 5 dagen/week
Post. obs. period: Direkt na blootstelling zijn dieren gedood en onderzocht
Doses: 25, 100, 400 ppm, 10/sex/groep
Control Group: yes, concurrent vehicle
Method: other
Year: 1990 **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Result: In summary, the exposure of Fischer 344 rats to methylethylketoxim for four weeks at target levels of 25, 100 and 400 ppm resulted in increased methemoglobin levels at 100 ppm (female rats) and at 400 ppm (rats). Significant alteration in the hematological parameters were also seen in the rats at 400 ppm. In addition at 400 ppm, increased organ weights were seen in the liver of the rats and in the spleen of the rats. However, there was no histologic correlate in the liver (only tissue examined). Therefore, this effect is equivocal. In the case of the spleen, this increase could represent a functional change in response to the hematological changes.
Source: SERVO DELDEN BV DELDEN

(77)

Species: rat **Sex:** male/female
Strain:
Route of admin.: inhalation
Exposure period: 28 days
Frequency of treatment: 6h/d and 5d/w
Post. obs. period:
Doses: 0.21, 1.02, 1.92, 2.57 mg/l
Control Group: yes
NOAEL: = 1.02 mg/l
LOAEL: = 1.92 mg/l
Method: other
Year: 1989 **GLP:** no data
Test substance: other TS
Remark: Study performed by DOW–Corning USA. Minor changes in hematological parameters at doses 1.92 mg/l and higher. Changes in organ weight (spleen, liver) at doses 1.92 mg/l and higher. Accumulation of iron in spleen at 1.92 mg/l and higher.
Source: DSM Special Products B.V. Geleen

(74)

Species: rat **Sex:** male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure period: 4 weeks
Frequency of treatment: 6h/d and 5d/w
Post. obs. period:
Doses: 25, 100, 400 ppm
Control Group: yes
NOAEL: = 25 ppm
LOAEL: = 100 ppm
Method: other
Year: 1990 **GLP:** yes
Test substance: other TS
Remark: The rats were exposed by inhalation to MEKO vapor. Exposure levels were analysed and particle size distribution measured. Ten animals/sex/group were used. At 100 ppm increased methemoglobin was observed in female rats. At 400 ppm significant alterations in most hematological parameters (increased methemoglobin, increased reticulocytes, increased platelets, increased MCW and MCH, increased total leucocytes counts, in addition decreased hemoglobin, hematocrit, erythrocytes and MCHC) were observed for both male and female rats. At 400 ppm remarcable erythrocyte morphology included increased numbers of nucleated erythrocytes and polychromia, were seen in male and female rats.
At 400 ppm increased absolute and relative organ weights of liver and spleen in males and females was seen.
Source: DSM Special Products B.V. Geleen

(78)

Species: rat **Sex:** male/female
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: 13 weeks
Frequency of treatment: 5 days/week
Post. obs. period:
Doses: 25, 75, 225 mg/kg/day
Control Group: yes
NOAEL: < 25 mg/kg
LOAEL: = 25 mg/kg
Method: other
Year: 1986 **GLP:** yes
Test substance: other TS
Remark: In this study 10 animals/sex/group were used. No mortality occurred. Dose related effects on hematological parameters and effects on organ weights of spleen and liver, no neurological effects. The primary target of the substance is the blood system with hemolytic anemia and compensatory hematopoiesis. Also extramedullary hemosiderosis (iron-accumulation) in the spleen was observed. On basis of the observed effects a NOEL of 10 mg/kg can be obtained by extrapolation.
Source: SERVO DELDEN BV DELDEN

(74)

Species: rat **Sex:** male/female
Strain:
Route of admin.: gavage
Exposure period: 13 weeks
Frequency of treatment: 5 days/week
Post. obs. period:
Doses: 40, 125, 400 mg/kg
Control Group: yes
NOAEL: < 40 mg/kg
LOAEL: = 40 mg/kg
Method: other
Year: 1991 **GLP:** yes
Test substance: other TS
Remark: In this subchronic neurotoxicity study (10-14 rats/ sex/group) effects on hematological parameters were seen again in all dose groups. The NOEL was estimated to be <40 mg/kg/day.
To check for neurotoxicity the standard "Functional Operational Battery", motor-activity data and neurohistopathology were performed. As positive control acrylamide was used.
At dose levels of 40 and 125 mg/kg/day no consistent or apparant treatment related change in neurobehavioral function or nervous system structure were seen. transient neurobehavioral changes occurred following dosing with 400 mg/kg/day, immediately after dosing, but these had resolved by the next day. No progressive long term, irreversible neurotoxicity was observed. The NOEL for neurotoxicity was set at 125 mg/kg/day.
Source: SERVO DELDEN BV DELDEN

(79)

Species: rat **Sex:** male
Strain: Fischer 344
Route of admin.: gavage
Exposure period: 28 days
Frequency of treatment: once daily
Post. obs. period: -
Doses: 0, 250, 500 mg/kg/day
Control Group: other: see remark 1
Method: other
Year: 1995 **GLP:** yes
Test substance: other TS
Remark: Control animals (15/group) received distilled water (negative control), 0.5% methylcellulose (vehicle control) or clofibric acid, 250 mg/kg (positive control), at the same dose volume as administered to the treated animals.
Result: Under the conditions of this study, MEKO did not produce any significant hepatic peroxisome proliferation in the rat, as indicated by a lack of effect on palmitoyl-CoA oxidation and by electron microscopy. The potential responsiveness of the

animals used in this study was confirmed by the marked induction of palmitoyl-CoA in the rats treated with clofibric acid. While MEKO was not a peroxisome proliferator in the rat, significant increases in the levels of hepatic glutathione (primarily reduced glutathione) were observed in rats given 250 and 500 mg/kg/day MEKO for 14 days. This lack of an effect after 7 days of dosing correlated with the hepatocellular hypertrophy which was seen microscopically after 14 and 28 but not 7 days of treatment.

Source: SERVO DELDEN BV DELDEN

(80)

Species: rat **Sex:** male/female
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: 13 weeks
Frequency of treatment: 5 days/week
Post. obs. period:
Doses: 25, 75, 225 mg/kg/day
Control Group: yes
NOAEL: < 25 mg/kg
LOAEL: = 25 mg/kg
Method: other
Year: 1986 **GLP:** yes
Test substance: other TS
Remark: In this study 10 animals/sex/group were used. No mortality occured. Dose related effects on hematological parameters and effects on organ weights of spleen and liver, no neurological effects.The primary target of the substance is the blood system with hemolytic anemia and compensatory hematopoiesis. Also extramedullaryhemosiderosis (iron-accumulation) in the spleen was observed. On basis of the observed effects a NOEL of 10 mg/kg can be obtained by extrapolation.

Source: DSM Special Products B.V. Geleen

(74)

Species: rat **Sex:** male/female
Strain:
Route of admin.: gavage
Exposure period: 13 weeks
Frequency of treatment: 5 days/week
Post. obs. period:
Doses: 40, 125, 400 mg/kg
Control Group: yes
NOAEL: < 40 mg/kg
LOAEL: = 40 mg/kg
Method: other
Year: 1991 **GLP:** yes
Test substance: other TS
Remark: In this subchronic neurotoxicity study (10–14 rats/ sex/group) effects on hematological parameters were seen again in all dose groups. The NOEL was estimated to be < 40 mg/kg/day.
To check for neurotoxicity the standard "Functional Operational Battery", motor–activity data and neurohistopathology were performed. As positive control acrylamide was used.
At dose levels of 40 and 125 mg/kg/day no consistent or apparant treatment related change in neurobehavioral function or nervous system structure were seen. transient neurobehavioral changes occurred following dosing with 400 mg/kg/day, immediately after dosing, but these had resolved by the next day. No progressive long term, irreversible neurotoxicity was observed. The NOEL for neurotoxicity was set at 125 mg/kg/day.
Source: DSM Special Products B.V. Geleen

(81)

Species: rat **Sex:** no data
Strain:
Route of admin.: oral unspecified
Exposure period: 13 weken
Frequency of treatment: geen gegevens
Post. obs. period: geen gegevens
Doses: 25, 75, 225 mg/kg/dag
Control Group: no data specified
LOAEL: 25 mg/kg
Method: other
Year: 1977 **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Source: SERVO DELDEN BV DELDEN

(82)

Species: mouse **Sex:** male/female
Strain: CD-1
Route of admin.: inhalation
Exposure period: 28 days
Frequency of treatment: 6h/d and 5d/w
Post. obs. period:
Doses: 25, 100, 400 ppm
Control Group: yes
NOAEL: = 100 ppm
LOAEL: = 400 ppm
Method: other
Year: 1990 **GLP:** yes
Test substance: other TS
Remark: Same experiment as mentioned in 5.4.4. Only slight increased methemoglobin levels were seen in the 400 ppm group. The other hematological parameters were not significantly effected. In the 400 ppm group increased organ weights in spleen and adrenals.
Source: SERVO DELDEN BV DELDEN

(83)

Species: mouse **Sex:** male/female
Strain: CD-1
Route of admin.: inhalation
Exposure period: 4 weken
Frequency of treatment: 6 uur/dag, 5 dagen/week
Post. obs. period: Na blootstelling zijn dieren gedood en onderzocht
Doses: 25, 100, 400 ppm, 10/sex/groep
Control Group: yes, concurrent vehicle
Method: other
Year: 1990 **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Result: In summary, the exposure of CD-1 mice to methylethylketoxim for four weeks at target levels of 25,100 and 400 ppm resulted in increased methemoglobin levels at 400 ppm. In addition at 400 ppm, increased organ weights in the spleen of male mice and in adrenals of the male mice were seen. In the case of the spleen, this increase could represent a functional change in response to the hematological changes.
Source: SERVO DELDEN BV DELDEN

(77)

Species: mouse **Sex:** male/female
Strain: CD–1
Route of admin.: inhalation
Exposure period: 28 days
Frequency of treatment: 6h/d and 5d/w
Post. obs. period:
Doses: 25, 100, 400 ppm
Control Group: yes
NOAEL: = 100 ppm
LOAEL: = 400 ppm
Method: other
Year: 1990 **GLP:** yes
Test substance: other TS
Remark: Same experiment as mentioned in 5.4.4. Only slight increased methemoglobin levels were seen in the 400 ppm group. The other hematological parameters were not significantly effected. In the 400 ppm group increased organ weights in spleen and adrenals.
Source: DSM Special Products B.V. Geleen

(83)

Species: mouse **Sex:** male
Strain: CD–1
Route of admin.: gavage
Exposure period: 1, 2, 4, 13 weeks
Frequency of treatment: 6 h/d, 5 d/w
Post. obs. period: 13 weeks
Doses: 0, 3, 10, 30, 100 ppm
Control Group: yes, concurrent no treatment
NOAEL: ca. 3 ppm
Method: other
Year: 1995 **GLP:** yes
Test substance: other TS
Remark: This study was designed to further investigate the effect of MEKO on the olfactory epithelium of the mouse observed in the chronic inhalation carcinogenicity study conducted as part of the MEKO Test Rule. Specifically, the goals of this study were to establish a No Observable Effect Level (NOEL) for this effect, determine if the lesions were reversible (healing potential) with cessation of exposure, and map the extent of the injury to the olfactory epithelium. The mouse was chosen since it appears to be more sensitive to this effect than the rat.
In addition, the effect of MEKO on liver peroxisome proliferation and glutathione content were evaluated since effects on these end–points have been linked to liver tumors in rodents.
Result: Under the conditions of this study, inhalation exposure to 10, 30 or 100 ppm of methylethylketoxim for 6 hours/day, 5 day/week produced minimal to moderately severe olfactory epithelium degeneration in CD–1 mice. The incidence and severity of the degeneration was concentration dependent and not progressive over time with continued exposure. The

lesions were localized to the olfactory epithelium lining the dorsal meatus in the anterior portion of the nasal cavity. Large areas of olfactory epithelium laterally and posteriorly appeared unaffected. The effect was reversible with cessation of exposure with complete recovery observed within 4 weeks at 10 ppm and nearly complete recovery after 13 weeks at the higher concentrations. Three ppm was considered to be a NOEL.

Under the exposure conditions of this study, methylethylketoxim was not hepatic peroxisome prolifirator nor produced any ultrastructural changes in liver cells after 13 weeks of exposure at concentrations up to 100 ppm. However, significant increases in levels of hepatic non–protein sulphydryl groups (primarily reduced glutathione) were measured following MEKO exposures at 30 and 100 ppm.

Source: SERVO DELDEN BV DELDEN

(84)

Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Post. obs. period:
Doses:
Control Group:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA98, TA100, TA 2637 and E.Coli uvra/pKM101
Concentration:
Metabolic activation: with and without
Result: negative
Method: other
Year: 1986 **GLP:** no data
Test substance: other TS
Source: SERVO DELDEN BV DELDEN
DSM Special Products B.V. Geleen

(85)

Type: Mouse lymphoma assay
System of testing: Mouse lymphoma L5178Y TK+/–
Concentration: up to 5 mg/pl
Metabolic activation: with and without
Result: negative
Method: other
Year: 1988 **GLP:** no data
Test substance: other TS
Remark: The test was positive without metabolic activation, but negative with metabolic activation. For activation S9 homogenate of liver from male Fischer 344 rats and Syrian golden hamsters induced with Aroclor 1254, was used. The negative result in the presence of metabolizing system indicates that no mutagenicity in in–vivo will occur.
Source: SERVO DELDEN BV DELDEN

(86)

Type: Mouse lymphoma assay
System of testing: Mouse lymphoma L5178Y TK+/–
Concentration: up to 5 mg/pl
Metabolic activation: with
Result: negative
Method: other
Year: 1988 **GLP:** no data
Test substance: other TS
Remark: The test was positive without metabolic activation, but negative with metabolic activation. For activation S9 homogenate of liver from male Fischer 344 rats and syrian golden hamsters induced wth Aroclor 1254, was used. The negative result in the presence of metabolizing system indicates that no mutagenicity in in–vivo will occur.
Source: DSM Special Products B.V. Geleen

(87)

Type: Sister chromatid exchange assay
System of testing: Chinese hamster (CHO) cells
Concentration: tot 1%
Metabolic activation:
Result: negative
Method:
Year: **GLP:**
Test substance: other TS
Remark: An in vitro SCE assay was performed by AlliedSigal using Chinese hamster ovary (CHO) cells. The CHO cells were exposed to MEKO at concentrations as high as 1% both in the absence and presence of rat liver enzymes (S9). MEKO did not induce a significant increase in SCE frequency at any of the concentrations tested. MEKO did not cause an increase in SCE frequency in a similar study conducted under NTP.
Source: SERVO DELDEN BV DELDEN

(88)

Type: Unscheduled DNA synthesis
System of testing:
Concentration: 5000..0.15 ug/l
Metabolic activation:
Result: negative
Method: other
Year: **GLP:** yes
Test substance: other TS
Remark: Industrial Health Foundation, Inc.'s, test article, Methylethylketoxime (MEKO) supplied by Allied Signal, Inc., was tested in the rat hepatocyte Unscheduled DNA synthesis assay. The test article was tested at ten dose levels ranging from 5000 .. 0.15 ug/ml and was fully evaluated at 5 dose levels of 1500, 500, 150, 50, and 15 ug/ml.
Water was determined to be the vehicle of choice based on the solubility and stability determination of the test article and compatibility with the target cells. The test article was soluble in water at a maximum concentration of approximately 100 mg/ml.
The results of the UDS assay indicate that under the test conditions, the test article did not cause a significant increase in the unscheduled DNA synthesis as measured by the mean number of net nuclear grain counts (i.e., an increase of at least 5 counts over the vehicle control), at any dose level. In this study the positive control, DMBA, induced a significant increase in the mean number of net nuclear grain counts over that in the vehicle control. All criteria for a valid test were met.
Therefore, the test article is considered to be negative in this study.
Source: SERVO DELDEN BV DELDEN

(89)

Type: other: Chromosome aberrations
System of testing:
Concentration:
Metabolic activation: with and without
Result:
Method:
Year: **GLP:**
Test substance: other TS
Remark: MEKO did not cause an increase in chromosome aberrations in Chinese hamster ovary cells (CHO) in presence or absence of rat liver enzymes in a study conducted under NTP.
Source: SERVO DELDEN BV DELDEN

(90)

Type:
System of testing:
Concentration:
Metabolic activation:
Result:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

5.6 Genetic Toxicity 'in Vivo'

Type: Cytogenetic assay
Species: rat **Sex:** male/female
Strain: Sprague–Dawley
Route of admin.: gavage
Exposure period: Single dose
Doses: 300, 600, 1200 mg/kg
Result:
Method: other
Year: 1990 **GLP:** yes
Test substance: other TS
Remark: The high dose was set as the MTD. Bone marrow cells, arrested in metaphase and collected 6, 24, 48 hours after dosing, were examined microscopically for structural chromosome aberrations. No significant effects were seen, regardless of treatment or bone marrow collection time.
Source: SERVO DELDEN BV DELDEN

(91)

Type: Cytogenetic assay
Species: Drosophila melanogaster **Sex:** male
Strain:
Route of admin.: drinking water
Exposure period: 3 days
Doses: 7500 ppm
Result:
Method: other
Year: 1991 **GLP:** no data
Test substance: other TS
Result: It is concluded that MEKO does not induce mutations in the post–meiotic germ cells of Drosophila melanogaster when administered by feeding to adult males.
Source: SERVO DELDEN BV DELDEN

(92)

Type: Cytogenetic assay
Species: rat **Sex:** male/female
Strain: Sprague–Dawley
Route of admin.: drinking water
Exposure period: 1 dag
Doses: 300, 600, 1200 mg/kg
Result:
Method: other
Year: 1990 **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Result: The results of the assay indicate that under the conditions described in the report, 2–Butanonoxim did not induce chromosomal aberrations in bone marrow cells of male or female rats.
Source: SERVO DELDEN BV DELDEN

(93)

Type: Cytogenetic assay
Species: Drosophila melanogaster **Sex:** male
Strain:
Route of admin.: drinking water
Exposure period: 3 dagen
Doses: 7500 ppm
Result:
Method: other
Year: 1991 **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Result: It is concluded that 2–Butanonoxim does not induce mutations in the post–meiotic germ cells of Drosophila melanogaster when administered by feeding to adult males.
Source: SERVO DELDEN BV DELDEN

(94)

Type: Cytogenetic assay
Species: rat **Sex:** male/female
Strain: Sprague–Dawley
Route of admin.: gavage
Exposure period: Single dose
Doses: 300, 600, 1200 mg/kg
Result:
Method: other
Year: 1990 **GLP:** yes
Test substance: other TS
Remark: The high dose was set as the MTD. Bone marrow cells, arrested in metaphase and collected 6, 24, 48 hours after dosing, were examined microscopically for structural chromosome aberrations. No significant effects were seen, regardless of treatment or bone marrow collection time.
Source: DSM Special Products B.V. Geleen

(95)

Type: Micronucleus assay
Species: mouse **Sex:**
Strain:
Route of admin.:
Exposure period:
Doses:
Result:
Method: other
Year: 1993 **GLP:** no data
Test substance: other TS
Result: The National Toxicology Program annual plan for fiscal year 1994 indicates an in-vivo micronucleus test was completed on MEKO in 1993. The results of this test are indicated as negative suggesting that MEKO did not cause an increase in micronuclei in either peripheral blood or bone marrow cells.
Source: SERVO DELDEN BV DELDEN

(90)

Type:
Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Doses:
Result:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

5.7 Carcinogenicity

Species: rat **Sex:** male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure period: 26 months
Frequency of treatment: 6h/d and 5d/w
Post. obs. period: see remark 1
Doses: 0, 15, 75, 375 ppm, 80/sex/group, 4 groups
Result:
Control Group: yes, concurrent no treatment
Method: other
Year: 1993 **GLP:** yes
Test substance: other TS
Remark: Body weight measurements were recorded once pretest, weekly through week 13, monthly through week 113 and just prior to sacrifice.
Hematology and clinical chemistry parameters were evaluated for up to 10 animals/sex/group sacrificed at month 3, 12 and 18 and at study termination.
Differential white blood cell counts were analyzed for all survivors at month 12 and 18 and at termination of the study.

Following approximately 3, 12 and 18 months of exposure, up to 10 animals/sex/group were sacrificed, selected organs were weighed and organ/body and organ/brain weight ratios calculated.
Following approximately 26 months of exposure, all survivors were sacrificed, selected organs were weighed and organ/body and organ/brain weight ratios calculated.
Histopathological evaluation of selected tissues was performed for all Group I and IV animals and sentinel animals and all animals in Groups II and III which were found dead or sacrificed in a moribund condition prior to study termination. In addition, the eyes, liver, lungs, nasopharyngeal tissues, ovaries, spleen and testes were examined for all animals in Groups II and III.

Result: At termination of the study, in the control group survivorship was 34% in the males and 60% in the females. There was no difference in survivorship among any of the exposure groups including control.

There were no physical observations which were considered MEKO related. Ophthalmoscopic examinations of the animals found a treatment-exaggerated incidence of corneal dystrophy and opacities.
The dystrophic changes seen in the 374 ppm group were far more severe than in other groups. This increase was probably a result of MEKO exaggerating a strain-related condition already present.

Mean body weights and body weight gains from study initiation were significantly elevated by exposure to MEKO in both the males and the females. After 13 weeks of exposure, the 374 ppm males were 13% heavier than the control males and the females were 4% heavier.

At the 3 month sacrifice in the 374 ppm group, methemoglobin was elevated in the males from 0.4 to 1.2%; hemoglobin was decreased 4%; erythrocytes were decreased 7%; mean corpuscular volume was increased 2%; mean corpuscular hemoglobin concentration was decreased 4%; platelets were increased 25% and leukocyte counts were increased 6%. Similar effects were seen in the females. The differences were still statistically significantly different at 12 months in the 374 ppm group but tolerance or adaptation seemed to occur for the effects. Most were no longer significantly different by 18 months in the males or 24 months in both sexes.

MEKO-related increases in absolute and relative organ weights were seen in the liver, spleen and testes. At three months in the 374 ppm group, liver weights were elevated about 18% and spleen weights were elevated by about 33%. Tolerance or adaptation occurred and the liver and spleen differences decreased over time. However the increase in testes weight did not. At study termination the 374 ppm group's testes weighed 82% more than the control group's.

Treatment-related macroscopic findings were not observed at

3 or 12 months. At 18 months an increased incidence of red/tan discoloration of the liver and enlarged testes in treated animals appeared to be treatment related. In the chronic study (24 months and all unscheduled deaths), an increased incidence of red/tan discoloration and nodules/masses of the liver, enlarged testes, and opacity enlarged spleens in animals of Group IV appeared to be treatment related.

There were a number of treatment related microscopic findings. Congestion of the spleen with pigment in reticuloendothelial cells and extramedullary hematopoiesis appeared to be treatment related in the 374 ppm animals at 3 months, 12 months and 18 months sacrifices. However, at the terminal sacrifice these findings were masked by the high incidence of mononuclear cell leukemia in animals other than the 374 ppm animals and could not be evaluated.
Findings which appeared treatment related at 12 and 18 months and in the chronic study were seen in the liver and nasal turbinates. The liver changes were increased incidence of basophilic foci and hepatocellular vacuoles and decreased incidence of hyperplasia/proliferation of the biliary duct and peribiliary fibrosis. The turbinate changes were degenerative changes of olfactory epithelium eosinophilic/ basophilic material/erythrocytes in the lumen of nasal turbinate section 2, 3 and 4; and a decrease in the incidence of eosinophilic droplets in olfactory epithelium in treated animals. Further findings which appeared treatment related only in the chronic study animals were seen in the liver. The liver changes were increased incidence of hepatocellular carcinoma and adenoma and spongiosis hepatis.

In conclusion, under the exposure conditions of this study, MEKO was a liver oncogen in the male rat at 75 ppm.

Source: SERVO DELDEN BV DELDEN

(96)

Species: rat **Sex:** male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure period: 26 maanden
Frequency of treatment: 6 uur/dag, 5 dagen/week
Post. obs. period: zie remark 1
Doses: 0, 15, 75, 375 ppm, 80/sex/groep, 4 groepen
Result:
Control Group: yes, concurrent no treatment
Method: other
Year: 1993 **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Body weight measurements were recorded once pretest, weekly through week 13, monthly through week 113 and just prior to sacrifice.
Hematology and clinical chemistry parameters were evaluated for up to 10 animals/sex/group sacrificed at month 3, 12 and

18 and at study termination.
Differential white blood cell counts were analyzed for all survivors at month 12 and 18 and at termination of the study.
Following approximately 3, 12 and 18 months of exposure, up to 10 animals/sex/group were sacrificed, selected organs were weighed and organ/body and organ/brain weight ratios calculated.
Following approximately 26 months of exposure , all survivors were sacrificed, selected organs were weighed and organ/body and organ/brain weight ratios calculated.
Histopathological evaluation of selected tissues was performed for all Group I and IV animals and sentinel animals and all animals in Groups II and III which were found dead or sacrificed in a moribund condition prior to study termination. In addition , the eyes, liver, lungs, nasopharyngeal tissues, ovaries, spleen and testes were examined for all animals in Groups II and III.

Result: At termination of the study, in the control group survivorship was 34% in the males and 60% in the females. There was no difference in survivorship among any of the exposure groups including control.

There were no physical observations which were considered MEKO related except for opacities. Opthalmoscopic examinations of the animals found a dose-related increase in cataracts and a treatment-exaggerated incidence of corneal dystrophy.
The dystrophic changes seen in the 374 ppm group were far more severe than in other groups. This increase was probably a result of MEKO exaggerating a strain-related condition already present.

Mean body weights and body weight gains from study initiation were significantly elevated by exposure to MEKO in both the males and the females. After 13 weeks of exposure, the 374 ppm males were 13% heavier than the control males and the females were 4% heavier.

At the 3 month sacrifice in the 374 ppm group, methemoglobin was elevated in the males from 0.4 to 1.2%; hemoglobin was decreased 4%; erythrocytes were decreased 7%; mean corpuscular volume was increased 2%; mean corpuscular hemoglobin concentration was decreased 4%; platelets were increased 25% and leukocyte counts were increased 6%. Similar effects were seen in the females. The differences were still statistically significantly different at 12 months in the 374 ppm group but tolerance or adaptation seemed to occur for the effects. Most were no longer significantly different by 18 months in the males or 24 months in both sexes.

MEKO-related increases in absolute and relative organ weights were seen in the liver, spleen and testes. At three months in the 374 ppm group , liver weights were elevated about 18% and spleen weights were elevated by about 33%. Tolerance or adaptation occurred and the liver and spleen

differences decreased over time. However the increase in testes weight did not. At study termination the 374 ppm group's testes weighed 82% more than the control group's.

Treatment-related macroscopic findings were not observed at 3 or 12 months. At 18 months an increased incidence of red/tan discoloration of the liver and enlarged testes in treated animals appeared to be treatment related. In the chronic study (24 months and all unscheduled deaths), an increased incidence of red/tan discoloration and nodules/masses ofthe liver, enlarged testes, and opacity ofthe eyes in treated animals; and reduced incidence of enlarged spleens in animals of Group IV appeared to be treatment related.

There were a number of treatment related microscopic findings. Congestion of the spleen with pigment in reticuloendothelial cells and extramedullary hematopoiesis appeared to be treatment related in the 374 ppm animals at 3 months, 12 months and 18 months sacrifices. However, at the terminal sacrifice these findings were masked by the high incidence of mononuclear cell leukemia in animals other than the 374 ppm animals and could not be evaluated.
Findings which appeared treatment related at 12 and 18 months and in the chronic study were seen in the liver and nasal turbinates. The liver changes were increased incidence of basophilic foci and hepatocellular vacuoles and decreased incidence of hyperplasia/proliferation of the biliary duct and peribiliary fibrosis. The turbinate changes were degenerative changes of olfactory epithelium eosinophilic/ basophilic material/erythrocytes in the lumen of nasal turbinate section 2, 3, and 4; and a decrease in the incidence of eosinophilic droplets in olfactory epithelium in treated animals. Further findings which appeared treatment related only in the chronic study animals were the liver and eyes. The liver changes were increased incidence of hepatocellular carcinoma and adenoma and spongiosis hepatis. The eye changes were eosinophilic material and inflammatory cells in the anterior chamber, mineralization and neovascularization of the cornea, and cataracts.

In conclusion, under the exposure conditions of this study, MEKO was a liver oncogen in the male rat at 75 ppm.

Source: SERVO DELDEN BV DELDEN

(97)

Species: rat **Sex:** male/female
Strain: Fischer 344
Route of admin.: inhalation
Exposure period: 24 months
Frequency of treatment: 6h/d and 5d/w
Post. obs. period:
Doses: 15, 75, 375 ppm
Result:
Control Group: yes
Method: other
Year: 1993 **GLP:** yes
Test substance: other TS
Remark: The final report of this carcinogenicity study performed in the USA will not be available untill end of 1994. Only interim results are available so far.
80 rats/sex/group were used. No indications for carcinogenicity were found so far.
Source: DSM Special Products B.V. Geleen

(98)

Species: mouse **Sex:** male/female
Strain: CD-1
Route of admin.: inhalation
Exposure period: 18 months
Frequency of treatment: 6h/d and 5d/w
Post. obs. period: see remark 1
Doses: 0, 15, 75, 350 ppm, 60/sex/group, 4 groups
Result:
Control Group: yes, concurrent no treatment
Method: other
Year: 1993 **GLP:** yes
Test substance: other TS
Remark: Body weight measurements were recorded once pretest, weekly through week 13, monthly through week 79 and just prior to sacrifice.
Hematology and clinical chemistry parameters were evaluated for all animals sacrificed at month 12.
Differential white blood cell counts were analyzed for all survivors at month 12 and at termination of the study.
Following approximately 12 months of exposure, up to 10 animals/sex/group were sacrificed, selected organs were weighed and organ/body and organ/brain weight ratios calculated.
Following approximately 18 months of exposure, all survivors were sacrificed, selected organs were weighed and organ/body and organ/brain weight ratios calculated.
Result: At termination of the study, in the control group survivorship was 43% in the males and 61% in the females. There was no difference in survivorship among any of the exposure groups including control. The physical observations ophthalmoscopic and body weight results indicated no signs of any MEKO-related effects. At the 12 month interim sacrifice, methemoglobin was elevated from 0.2% in the

controls to 0.5% in the 374 ppm group males.
In the females methemoglobin did not appear to be effected but there was an increase in platelets in the 374 ppm group (35%) and a significant decrease in mean corpuscular hemoglobin concentration at 76 ppm (2.7%) and 374 ppm (3.3%). Statistically significant changes were seen in some clinical chemistry parameters evaluated at the 12 month interim sacrifice. In the 374 ppm group males, there was an decrease in chloride (4%), and increase in creatinine (50%), and increase in total protein (18%) and an increase in albumin (32%). None of these parameters were changed in the females or showed a dose–related increase. However, because they occurred in the high–exposure group they may be MEKO related.
At the 12 month interim sacrifice, liver organ weights were significantly increased (17%) in the females at 374 ppm. At termination of the study there were no related effects on organ weights.
There were no MEKO related macroscopic findings.
Microscopically, findings which appeared to be related to treatment included changes in the nasal turbinates and in the liver. In the turbinates, degenerative and reparative changes were observed. These included desquamation of olfactory epithelium, dilation of submucosal glands debris and inflammatory cells in the gland and in the nasal lumen and with proliferation of squamous or respiratory epithelium. In some areas the hypertrophic cells from the glands appeared to be extending to the luminal surface and replacing the lost epithelium.
A NOEL for this finding could not be obtained.

The liver changes, indicating hepatoxicity, included pigment in reticuloendothelial cells, necrosis, centrilobular, hepatocellular hypertrophy and granulomatous inflammation. There was also an increase in liver carcinomas in the 374 ppm male group relative to control and the exposure groups.

In conclusion, under the exposure conditions of this study, MEKO produced changes in the olfactory epithelium in all exposed groups in both sexes and was a liver oncogen in male CD–1 mice at 374 ppm.

Source: SERVO DELDEN BV DELDEN

(99)

Species: mouse **Sex:** male/female
Strain: CD-1
Route of admin.: inhalation
Exposure period: 18 maanden
Frequency of treatment: 6 uur/dag, 5 dagen/week
Post. obs. period: zie remark 1
Doses: 0, 15, 75, 375 ppm , 60 /sex/groep, 4 groepen
Result:
Control Group: yes, concurrent no treatment
Method: other
Year: 1993 **GLP:** no data
Test substance: as prescribed by 1.1 - 1.4
Remark: Body weight measurements were recorded once pretest, weekly through week 13, monthly through week 79 and just prior to sacrifice.
Hematology and clinical chemistry parameters were evaluated for all animals sacrificed at month 12.
Differential white blood cell counts were analyzed for all survivors at month 12 and at termination of the study.
Following approximately 12 months of exposure, up to 10 animals/sex/group were sacrificed, selected organs were weighed and organ/body and organ/brain weight ratios calculated.
Following approximately 18 months of exposure , all survivors were sacrificed, selected organs were weighed and organ/body and organ/brain weight ratios calculated.
Result: At termination of the study, in the control group survivorship was 43% in the males and 61 % in the females. There was no difference in survivorship among any of the exposure groups including control. The physical observations, opthalmoscopic and body weight results indicated no signs of any MEKO-related effects. At the 12 month interim sacrifice, methemoglobin was elevated from 0.2% in the controls to 0.5% in the 374 ppm group males. In the females methemoglobin did not appear to be effected but there was an increase in platelets in the 374 ppm group (35%) and a significant decrease in mean corpuscular hemoglobin concentration at 76 ppm (2.7%) and 374 ppm (3.3%). Statistically significant changes were seen in some clinical chemistry parameters evaluated at the 12-month interim sacrifice. In the 374 ppm group males, there was an decrease in chloride (4%), and increase in creatinine (50%), and increase in total protein (18%) and an increase in albumin (32%). None of these parameters were changed in the females or showed a dose-related increase. However, because they occurred in the high-exposure group they may be MEKO related.
At the 12-month interim sacrifice, liver organ weights were significantly increased (17%) in the females at 374 ppm. At termination of the study there were no related effects on organ weights.
There were no MEKO related macroscopic findings.
Microscopically, findings which appeared to be related to treatment included changes in the nasal turbinates and in the liver. In the turbinates, degenerative and reparative

changes were observed. These included desquamation of olfactory epithelium, dilation of submucosal glands debris and inflammatory cells in the gland and in the nasal lumen and with proliferation of squamous or respiratory epithelium. In some areas the hypertrophic cells from the glands appeared to be extending to the luminal surface and replacing the lost epithelium.
A NOEL for this finding could not be obtained.

The liver changes, indicating hepatoxicity, included pigment in reticuloendothelial cells, necrosis, centrilobular, hepatocellular hypertophy and granulomatous inflammation. There was also an increase in liver carcinomas in the 374 ppm male group relative to control and the exposure groups.

In conclusion, under the exposure conditions of this study, MEKO produced changes in the olfactory epithelium in all exposed groups in both sexes and was a liver oncogen in male CD-1 mice at 374 ppm.

Source: SERVO DELDEN BV DELDEN

(100)

Species: mouse **Sex:** male/female
Strain: CD-1
Route of admin.: inhalation
Exposure period: 18 months
Frequency of treatment: 6h/d and 5d/w
Post. obs. period:
Doses: 15, 75, 350 ppm
Result:
Control Group: yes
Method: other
Year: 1993 **GLP:** yes
Test substance: other TS
Remark: The same study as 5.7.1. At 375 ppm microscopic examination revealed degenerative changes in the olfactory epithelium with respiratory or squamous adaptive metaplasia in the turbinates sections. Whether these effects also occur at lower dose is under investigation.
Source: DSM Special Products B.V. Geleen

(101)

Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Post. obs. period:
Doses:
Result:
Control Group:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

5.8 Toxicity to Reproduction

Type: Two generation study
Species: rat **Sex:** male/female
Strain: Sprague–Dawley
Route of admin.: gavage
Exposure Period: 13 weeks
Frequency of treatment: once daily
Premating Exposure Period
male: 10 weeks
female: 10 weeks
Duration of test:
Doses: 10, 100, 200 mg/kg
Control Group: yes
NOAEL Parental: < 10 mg/kg bw
NOAEL F1 Offspr.: = 200 mg/kg bw
NOAEL F2 Offspr.: = 200 mg/kg bw
Method: other
Year: 1992 **GLP:** yes
Test substance: other TS
Remark: Male and female CD Sprague–Dawley weanling rats (F0) were administered MEKO in deionised/distilled water by gavage at 0, 10, 100, 200 mg/kg/d at a dosing volume of 2.0 ml/kg, 30 animals/sex/dose, for 10 weeks. Animals were than randomly mated for a three week mating period to produce the F1, with dosing continued. Selected F1 weanlings, 30/sex/dose, were administered MEKO and mated as above.
Hematologic evaluations and histopathology were performed.
Result: Adult toxicity was observed in both generations and in both sexes at all doses of MEKO with clear dose–related incidences and severity of findings. Consistent evidence of treatment related anemia was observed at 200 mg/kg/d with concomitant histologic evidence of extramedullary hematopoiesis and hemosiderosis in adult livers and spleens; spleen weights were increased at this dose level as well. At 100 mg/kg/d, these effects were also seen. At 10 mg/kg/d only histologic evidence of extramedullary hematopoiesis and hemosiderosis was observed in spleens and livers of F0 and

F1 males and females. Therefore no NOEL for adult toxicity could be established.
There was no evidence of reproductive organ or mammary gland histopathology at any dose tested. There was no evidence of reproductive or postnatal toxicity at any dose tested.
There was no "no observable adverse effect level" (NOAEL) detected for adult toxicity in this study due to histologic evidence of hepatic and splenic involvement at the low dose. The NOAEL for this reproductive and postnatal toxicity was at least 200 mg/kg/d under the conditions of this study.

Source: SERVO DELDEN BV DELDEN

(102)

Type: Two generation study
Species: rat **Sex:** male/female
Strain: Sprague–Dawley
Route of admin.: drinking water
Exposure Period: 10 weken
Frequency of treatment: 2 ml/kg/dag
Premating Exposure Period
male: 10 weken
female: 10 weken
Duration of test: 2 generaties
Doses: 0, 10, 100, 200 mg/kg/dag, doseringsvolume 2,0 ml/kg, 30 dieren/sex/dose
Control Group: yes, concurrent vehicle
Method: other
Year: 1990 **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Result: Adult toxicity was observed in both generations and in both sexes at all doses of MEKO with clear dose–related incidences and severity of the findings. At 200 mg/kg/day, adult mortality occurred with consistent reduction in body weight and food consumption during the F0 and F1 prebreed exposure periods; clinical signs of toxicity were also consistently observed.
Consistent evidence of treatment–related anemia was observed at 200 mg/kg/day with concomitant histologic evidence of extramedullary hematopoieses and hemosiderosis in adult livers and spleens; spleen weights were increased at this dose as well. At 100 mg/kg/day, body weights and food consumption were occasionally reduced, and clinical signs of toxicity were observed. Anemia was also observed at this dose with associated liver and spleen histopathology and increased spleen weights; no treatment–related mortality occurred at this dose. At 10 mg/ kg/day, only the histologic evidence of extramedullary hematopoieses and hemosiderosis was observed in spleens and livers. There was no evidence of reproductive organ or mammary gland histopathology at any dose tested. There was no evidence of reproductive toxicity or of postnatal toxicity at any dose tested.

There was no "no observable adverse effect level" (NOAEL) detected for adult toxicity in this study due to histologic evidence of hepatic and splenic involvement at the low dose. The NOAEL for this reproductive and postnatal toxicity was

at least 200 mg/kg/day under the conditions of this study.
Source: SERVO DELDEN BV DELDEN

(103)

Type: Two generation study
Species: rat **Sex:** male/female
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure Period: 13 weeks
Frequency of treatment: once daily
Premating Exposure Period
male: 10 weeks
female: 10 weeks
Duration of test:
Doses: 10, 100, 200 mg/kg
Control Group: yes
NOAEL Parental: < 10 mg/kg bw
NOAEL F1 Offspr.: = 200 mg/kg bw
NOAEL F2 Offspr.: = 200 mg/kg bw
Method: other
Year: 1992 **GLP:** yes
Test substance: other TS
Remark: Male and female CD Spraque-Dawley weanling rats (F0) were administered MEKO in deionised/distilled water by gavage at 0, 10, 100, 200 mg/kg/d at a dosing volume of 2.0 ml/kg, 30 animals/sex/dose, for 10 weeks. Animals were than randomly mated for a three week mating period to produce the F1, with dosing continued. Selected F1 weanlings, 30/sex/dose, were administered MEKO and mated as above.
Hematologic evaluations and histopathology were performed. Adult toxicity was observed in both generations and in both sexes at all doses of MEKO with clear dose-related incidences and severity of findings. Consistent evidence of treatment related anemia was observed at 200 mg/kg/d with concomitant histologic evidence of extramedullary hematopoiesis and hemosiderosis in adult livers and spleens; spleen weights were increased at this dose level as well. At 100 mg/kg/d, these effcets were also seen. At 10 mg/kg/d only histologic evidence of extramedullary hematopoiesis and hemosiderosis was observed in spleens and livers of F0 and F1 males and females. Therefore no NOEL for adult toxicity could be established.
There was no evidence of reproductive organ or mammary gland histopathology at any dose tested. There was no evidence of reproductive or postnatal toxicity at any dose tested. Therefore the NOEL for reproductive and postnatal toxicity was at least 200 mg/kg/d.
Source: DSM Special Products B.V. Geleen

(104)

Type:
Species: **Sex:**
Strain:
Route of admin.:
Exposure Period:
Frequency of treatment:
Duration of test:
Doses:
Control Group:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

5.9 Developmental Toxicity/Teratogenicity

Species: rat **Sex:** female
Strain:
Route of admin.: drinking water
Exposure period: dag 6 tot en met dag 15
Frequency of treatment: 10ml/kg/dag
Duration of test: dag 0 tot en met dag 20
Doses: 60, 200, 600 mg/kg/dag, doseringsvolume 10 ml/kg, 3*25 dieren
Control Group: yes, concurrent vehicle
Method: other
Year: 1990 **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Result: Oral administration of 2–Butanonoxim to pregnant rats for ten consecutive days produced maternal toxicity as expressed through post–dosing clinical signs and body weight and food consumption effects at dosage levels of 200 and 600 mg/kg/day. 2–Butanonoxim was not developmentally toxic or teratogenic at any of the dosage levels tested
Source: SERVO DELDEN BV DELDEN

(105)

Species: rabbit **Sex:** female
Strain: New Zealand white
Route of admin.: drinking water
Exposure period: Dag 6 tot en met dag 18
Frequency of treatment: 2 ml/kg/dag
Duration of test: dag 0 tot en met dag 29
Doses: 8, 14, 24, 40 mg/kg/dag, doseringsvolume 2 ml/kg/dag, 4*18 dieren
Control Group: yes, concurrent vehicle
NOAEL Maternalt.: 14 mg/kg bw
Method: other
Year: 1990 **GLP:** no data
Test substance: as prescribed by 1.1 – 1.4
Remark: Test performed by Springborn Laboratories, Inc. (SLS) Spencerville USA
Result: Oral administration of 2–Butanonoxim to pregnant rabbits produced dose–dependent maternal toxicity at levels of 24 and 40 mg/kg/day. A dosage level of 14 mg/kg/day was considered a no effect level for maternal toxicity. Excessive mortality and abortion in the 40 mg/kg/day group (11/18) precluded any meaningful assessment of the Ceasarean section data. 2–Butanonoxim was not developmentally toxic or teratogenic at dosage levels up to 24 mg/kg/day.
Source: SERVO DELDEN BV DELDEN

Species: rat **Sex:** female
Strain:
Route of admin.: gavage
Exposure period: from gestation day 6 through gestation day 15
Frequency of treatment: once dayly
Duration of test: day 0 through day 20
Doses: 60, 200, 600 mg/kg, dosagevolume 10 ml/kg/day, 3*25 animals
Control Group: yes, concurrent vehicle
NOAEL Maternalt.: = 60 mg/kg bw
NOAEL Teratogen.: = 600 mg/kg bw
Method: other
Year: 1990 **GLP:** yes
Test substance: other TS
Remark: The objective of this study was to evaluate the embryotoxic and teratogenic effects of MEKO administered to pregnant rats during the period of major organogenesis.
25 females/dose group were treated with MEKO by gavage and a dosage volume of 10 ml/kg. Vehicle was distilled water.
Clinical signs of toxicity and body weights and food consumption were investigated. Cesarean sections were performed on gestation day 20. Intrauterine survival was evaluated and the fetuses were sexed, weighed and examined for external, visceral and skeletal abnormalities.
Clinical signs of toxicity were observed at 200 and 600 mg/kg. These clinical signs were generally transient and had disappeared before dosing on the following day.
Also body weight losses and/or reduced body weight gain and reduced food consumption was seen in these dose groups.
No treatment–related effects on development and teratogenicity occurred. The NOEL was therefore 600 mg/kg/d.

Result: Oral administration of MEKO to pregnant rats for ten consecutive days produced maternal toxicity as expressed to post-dosing clinical signs and body-weight and food consumption effects at dosage levels of 200 and 600 mg/kg/day. MEKO was not developmentally toxic or teratogenic at any of the dosage levels tested.
Source: SERVO DELDEN BV DELDEN

(106)

Species: rat **Sex:** female
Strain:
Route of admin.: gavage
Exposure period: from gestation day 6 through gestation day 15
Frequency of treatment: once daily
Duration of test:
Doses: 60, 200, 600 mg/kg
Control Group: yes
NOAEL Maternalt.: = 60 mg/kg bw
NOAEL Teratogen.: = 600 mg/kg bw
Method: other
Year: 1991 **GLP:** yes
Test substance: other TS
Remark: The objective of this study was to evaluate the embryotoxic and teratogenic effects of MEKO administered to pregnant rats during the period of major organogenesis.
25 females/dose group were treated with MEKO by gavage and a dosage volume of 10 ml/kg. Vehicle was distilled water.
Clinical signs of toxicity and body weights and food consumption were investigated. Cesarean sections were performed on gestation day 20. Intrauterine survival was evaluated and the fetuses were sexed, weighed and examined for external, visceral and skeletal abnormalities.
Clinical signs of toxicity were observed at 200 and 600 mg/kg. These clinical signs were generally transient and had disappeared before dosing on the following day.
Also body weight losses and/or reduced body weight gain and reduced food consumption was seen in these dose groups.
No treatment-related effects on development and teratogenicity occured. The NOEL was therefore 600 mg/kg/d.
Source: DSM Special Products B.V. Geleen

(107)

Species: rabbit **Sex:** female
Strain: New Zealand white
Route of admin.: gavage
Exposure period: from gestation day 6 through gestation day 18
Frequency of treatment: once daily
Duration of test: day 0 through day 29
Doses: 8, 14, 24, 40 mg/kg, dosagevolume 2 ml/kg/day, 4*18 animals.
Control Group: yes, concurrent vehicle
NOAEL Maternalt.: = 14 mg/kg bw
NOAEL Teratogen.: = 40 mg/kg bw
Method: other
Year: 1990 **GLP:** yes
Test substance: other TS
Remark: Similar study as described in 5.9.1
18 animals/dose group were used. Dosevolume 2 ml/kg. Vehicle distilled water. Clinical signs of toxicity were seen at 40 mg/kg/d. Three females aborted and eight females were found dead at the 40/mg/kg/d level between gestation day 11 and 24. All other females survived. Gross–abnormalities and internal findings (lungs, liver, stomach, urinary bladder), were seen in the females that were found dead.
Dose–dependent maternal toxicity was therefore seen at 24 and 40 mg/kg/d. The NOEL was set at 18 mg/kg/d.
Excessive mortality and abortion in the high dose group precluded any meaningful assessment of the Cesarean section. The NOEL for development and teratogenicity was therefore set at 24 mg/kg/d.
Result: Oral administration of MEKO to pregnant rabbits produced dose–dependent maternal toxicity at levels of 24 and 40 mg/kg/day.
A dosage level of 14 mg/kg/day was considered a No Effect Level for maternal toxicity.
Excessive mortality and abortion in the 40 mg/kg/day group (11/18) precluded any meaningful assessment of the Cesarean section data.
MEKO was not developmentally toxic or teratogenic at dosage levels up to 24 mg/kg/day.
Source: SERVO DELDEN BV DELDEN

(108)

Species: rabbit **Sex:** female
Strain: New Zealand white
Route of admin.: gavage
Exposure period: from gestation day 6 through gestation day 18
Frequency of treatment: once daily
Duration of test:
Doses: 8, 14, 24, 40 mg/kg
Control Group: yes
NOAEL Maternalt.: = 14 mg/kg bw
NOAEL Teratogen.: = 40 mg/kg bw
Method: other
Year: 1991 **GLP:** yes
Test substance: other TS
Remark: Similar study as described in 5.9.1
18 animals/dose group were used. Dosevolume 2 ml/kg. Vehicle distilled water. Clinical signs of toxicity were seen at 40 mg/kg/d. Three females aborted and eight females were found dead at the 40/mg/kg/d level between gestation day 11 and 24. All other females survived. Gross-abnormalities and internal findings (lungs, liver, stomach, urinary bladder), were seen in the females that were found dead.
Dose-dependent maternal toxicity was therefore seen at 24 and 40 mg/kg/d. The NOEL was set at 18 mg/kg/d.
Excessive mortality and abortion in the high dose group precluded any meaningful assessment of the cesarian section. The NOEL for development and teratogenicity was therefore set at 24 mg/kg/d.
Source: DSM Special Products B.V. Geleen

(109)

Species: **Sex:**
Strain:
Route of admin.:
Exposure period:
Frequency of treatment:
Duration of test:
Doses:
Control Group:
Method:
Year: **GLP:**
Test substance:
Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

5.10 Other Relevant Information

Type: Biochemical or cellular interactions
Remark: In animals oximes, among others MEKO, are able to inhibit acetaldehyde dehydrogenase. This inhibition seems reversible. Ethylalcohol use after have been exposed to oximes might result in increased acetaldehyde concentrations in the body, giving rise to effects like rapid pulse, nausea, red face (the so called antabuse-effect).
Source: SERVO DELDEN BV DELDEN

Type: Biochemical or cellular interactions
Remark: Normally ethylalcohol is metabolised in humans to acetaldehyde which is metabolised to acetc acid. Oximes, among others MEKO, are able to inhibit acetaldehyde dehydrogenase. This inhibition seems reversible. Ethylalcohol use after have been exposed to oximes may result in high acetaldehyde concentrations in the body, giving rise to effects like rapid pulse, nausea, red face (the so called antabuse–effect).
Source: DSM Special Products B.V. Geleen

Type: other
Remark: The oxime MEKO (and also several other oximes) are known to affect primarily the bloodsystem (see also 5.4 and 5.8 data). It affects hematological parameters. Hemolytic anemia like effects are seen with compensatory hematopoiesis. Also at high chronic dose, hemosiderosis is observed in the spleen with acompanied spleen enlargement. These effects appeare reversible when exposure is stopped.
Source: DSM Special Products B.V. Geleen

Type:
Source: SERVO DELDEN BV DELDEN

5.11 Experience with Human Exposure

Remark: no disponible
Source: UNION DERIVAN S.A. VILADECANS

Remark: Es liegen keine Untersuchungsberichte der BASF vor.
Source: BASF AG Ludwigshafen

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(33) Allied Signal USA in house data.

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7.1 Risk Assessment

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